NIH: Future, Plans, Priorities

CSRAC
May 2, 2011

Lawrence A. Tabak, D.D.S., Ph.D.

Principal Deputy Director

National Institutes of Health

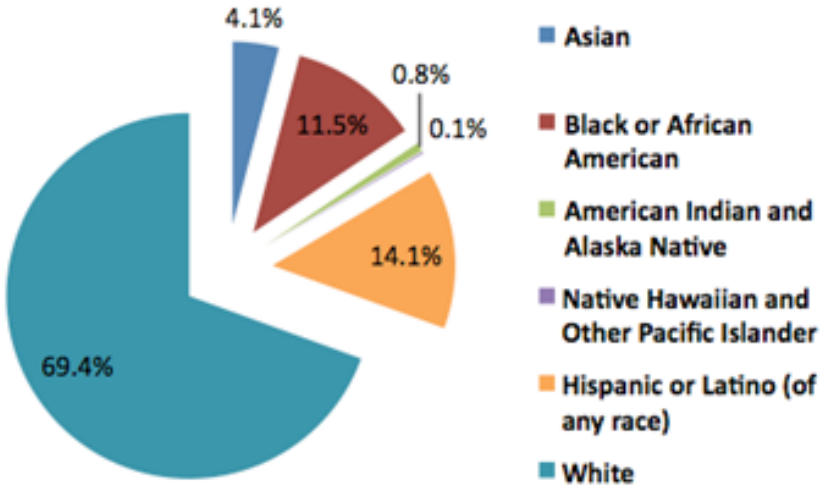
NIH: Future, Plans, Priorities

- **An Environmental Scan**
- Translational and Therapeutics Research at NIH
- Substance Use, Abuse, and Addiction Research at NIH

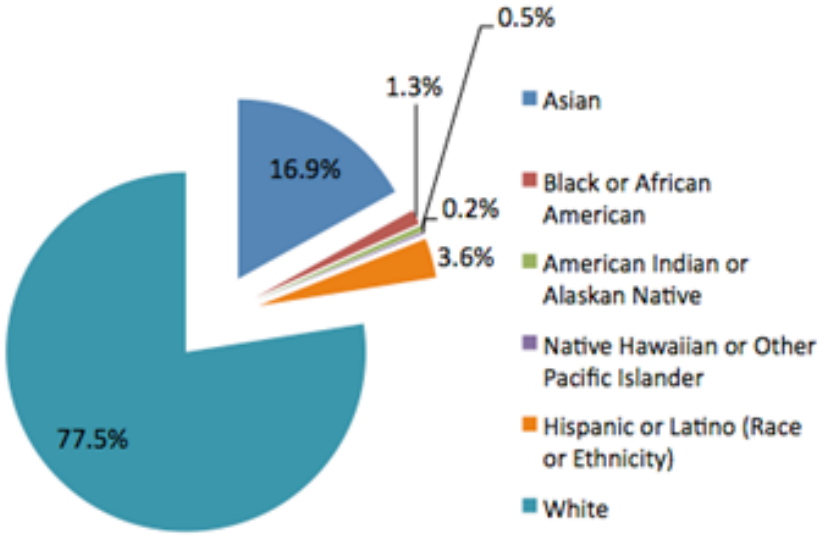
Diversity of the NIH-Funded Workforce

NIH has had a less than impressive impact on the diversity of the NIH-funded scientific workforce over the past 30+ years.

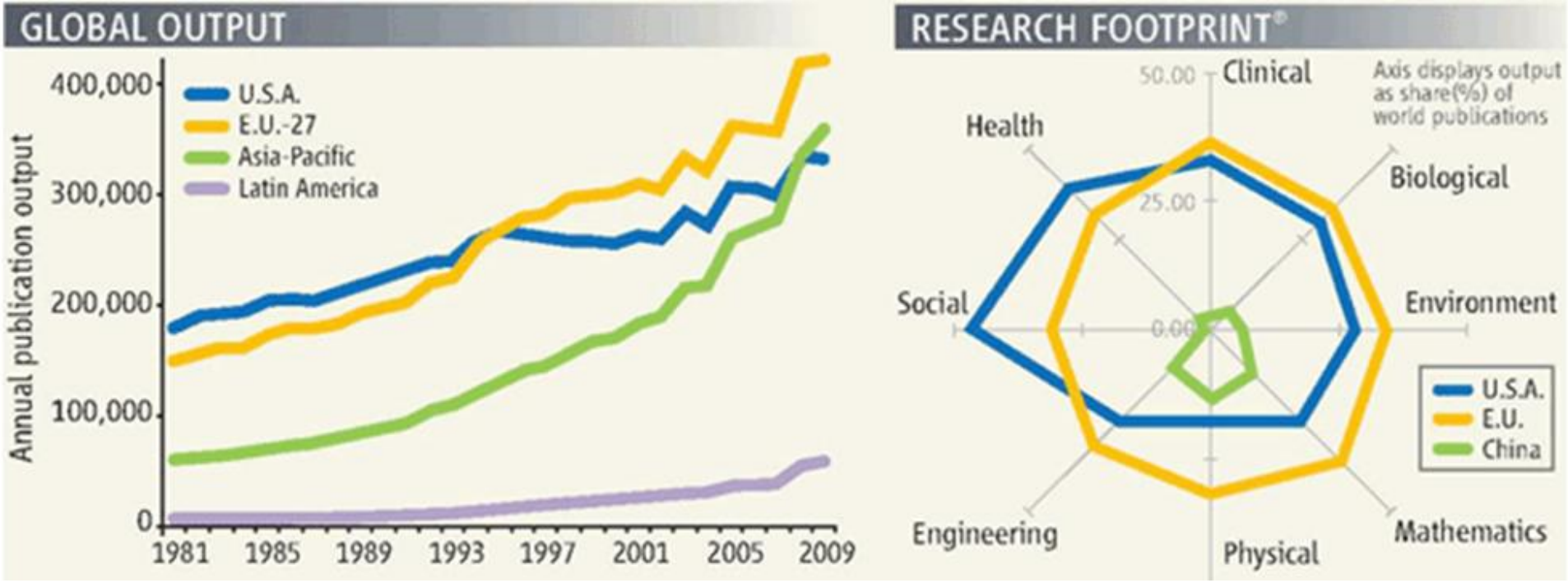
2008 United States Census Bureau reports on Race and Ethnicity



FY 2009 Race and Ethnicity of Reporting Principal Investigators on Research Project Grants



Science, Technology, Engineering, and Mathematics Trends



Mervis, J., Science 330:1032, 2010.

Science, Technology, Engineering, and Mathematics Trends

- The United States ranks just 29th out of 109 countries in the percentage of 24 year olds with a math or science degree.
- As ITIF documented in its The Atlantic Century report, the United States ranks 6th out of 40 nations on innovation-based competitiveness (e.g., corporate R&D, venture capital, scientists and engineers), and most troubling the United States ranks 40th of 40 nations in the rate of progress over the last decade.

U.S. Department of Health and Human Services
NIH News
National Institutes of Health

The Office of the Director (OD)

For Immediate Release
Wednesday, April 27, 2011

Contact:
NIH Office of Communications
301-496-5787

NIH establishes working group on the future biomedical research workforce

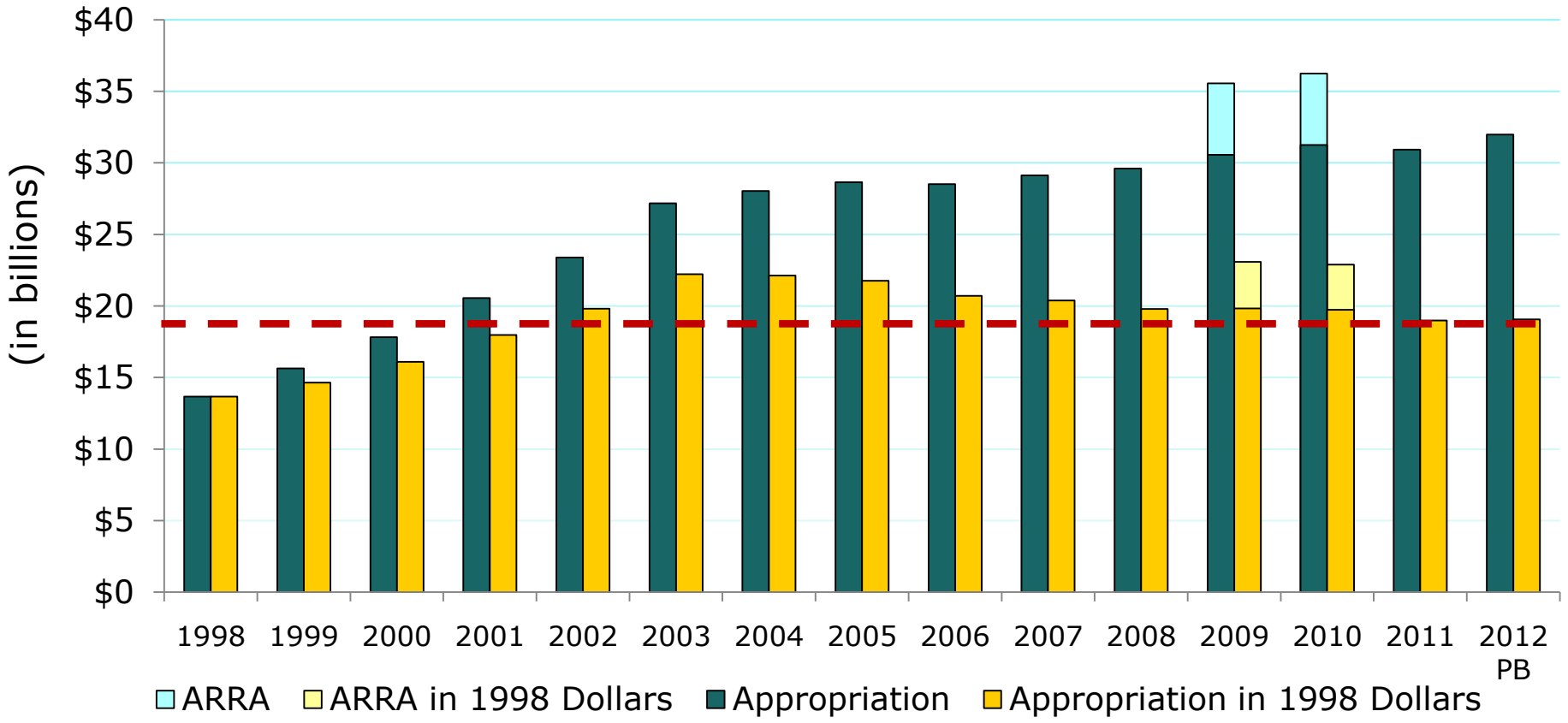
A new working group at the National Institutes of Health will examine the future of the biomedical research workforce in the United States. The group will recommend actions to the Advisory Committee to the Director to ensure a diverse and sustainable biomedical and behavioral research workforce. The working group will consider questions such as:

- What is the right size of the workforce?
- What are the appropriate types of positions that should be supported to allow people to have successful careers and to continue to advance biomedical and behavioral sciences?
- What is the best way to support these various positions?
- What types of training should be provided?

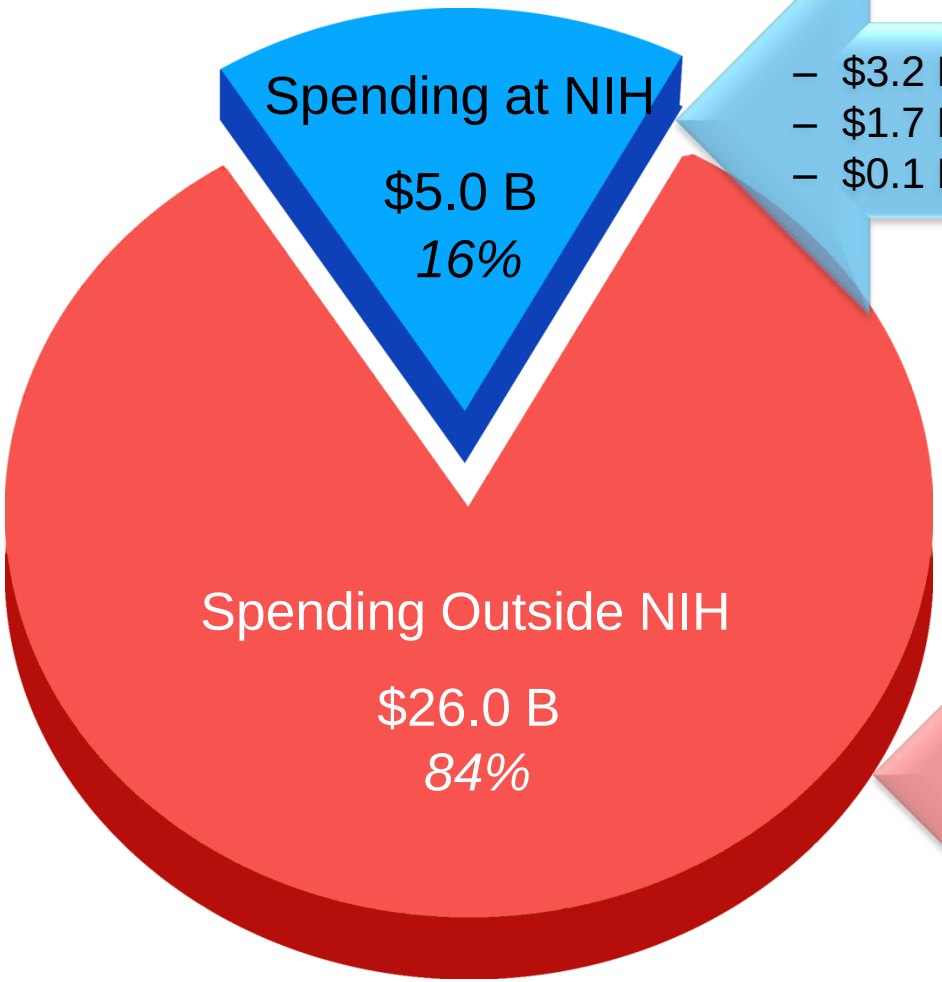
NIH: Future, Plans, Priorities

- **An Environmental Scan**
- Translational and Therapeutics Research at NIH
- Substance Use, Abuse, and Addiction Research at NIH

The Effects of Inflationary Growth on Purchasing Power: NIH Appropriation vs. Appropriation in 1998 Dollars (FY 2012 Total Program Request)



NIH Extramural & Intramural Funding (FY 2010 Budget)

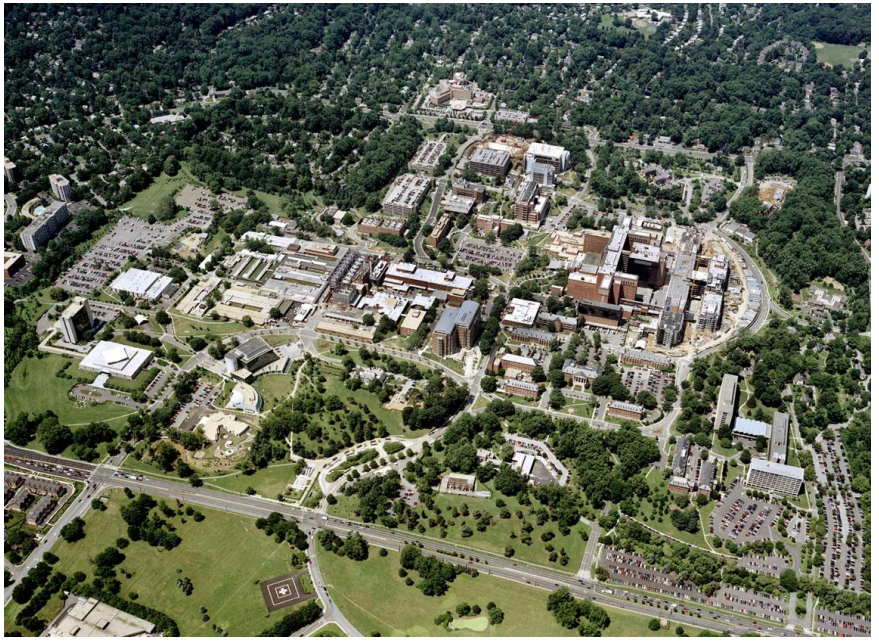


- $3.2 B Intramural Research
- $1.7 B Research Management & Support
- $0.1 B Buildings and Facilities

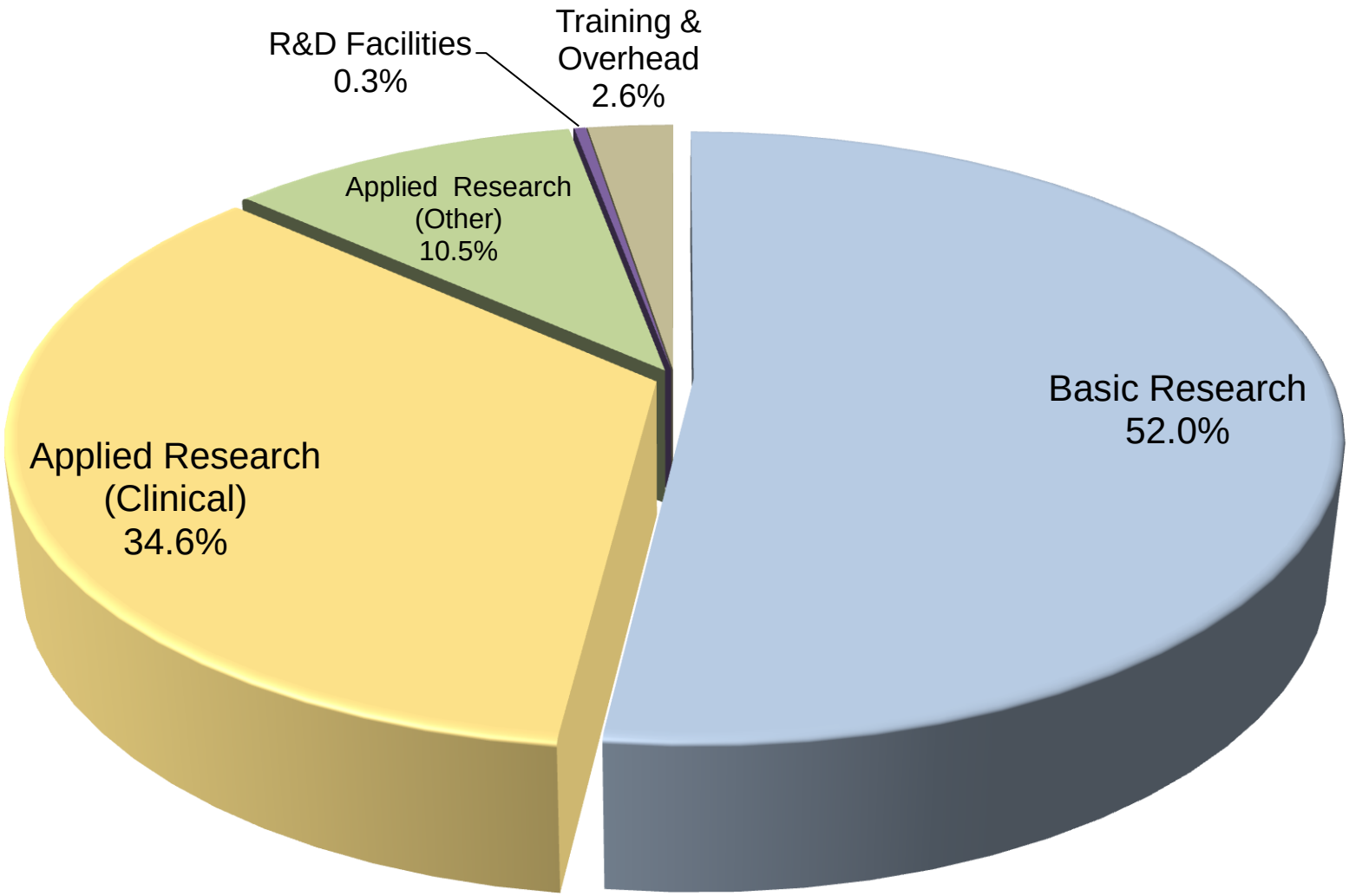
- Supports over 325,000 Scientists & Research Personnel
- Supports over 3,000 Institutions

NIH: Future, Plans, Priorities

- Why Research Matters
- **Translational and Therapeutics Research at NIH**
- Substance Use, Abuse, and Addiction Research at NIH



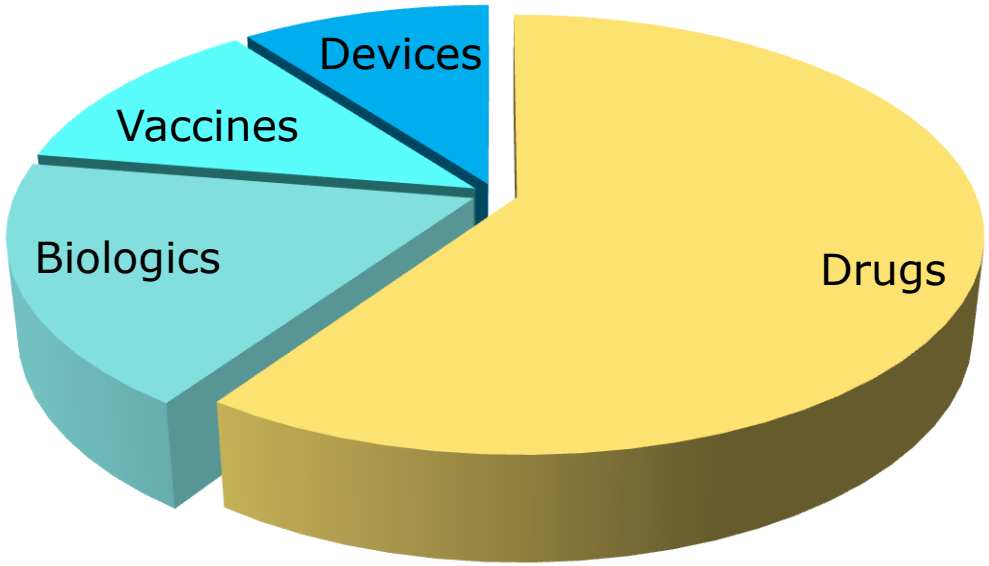
FY 2010 Percent Distribution of Basic and Clinical Research



Therapeutics Development at NIH

A 2010 trans-NIH inventory of activities relevant to therapeutics development found:

- Substantial investments in therapeutics development research
- Approximately 65% preclinical research; 35% clinical research
- 550 activities reported of varying sizes and areas of emphasis



N Engl J Med 2011;364:535-41.

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

The Role of Public-Sector Research in the Discovery of Drugs and Vaccines

Ashley J. Stevens, D.Phil., Jonathan J. Jensen, M.B.A., Katrine Wyller, M.B.E., Patrick C. Kilgore, B.S., Sabarni Chatterjee, M.B.A., Ph.D., and Mark L. Rohrbaugh, Ph.D., J.D.

RESULTS

We found that during the past 40 years, 153 new FDA-approved drugs, vaccines, or new indications for existing drugs were discovered through research carried out in PSRIs.

PSRI-discovered drugs are expected to have a disproportionately large therapeutic effect.

Table 1. Number of Drug Products Approved by the Food and Drug Administration and Originating from Public-Sector Research, According to Therapeutic Area, 1970–2009.

Therapeutic Area	Number
Total	153
Hematology or oncology	40
Infectious disease	36
Cardiology	12
Metabolic disease	12
Central nervous system	12
Dermatology	7
Renal disease	7
Ophthalmology	6
Immunology	6
Gastroenterology	4
Women's health	3
Allergy	2
Pulmonary disease	2
Urology	2
Anesthesiology	1
Dental disorders	1

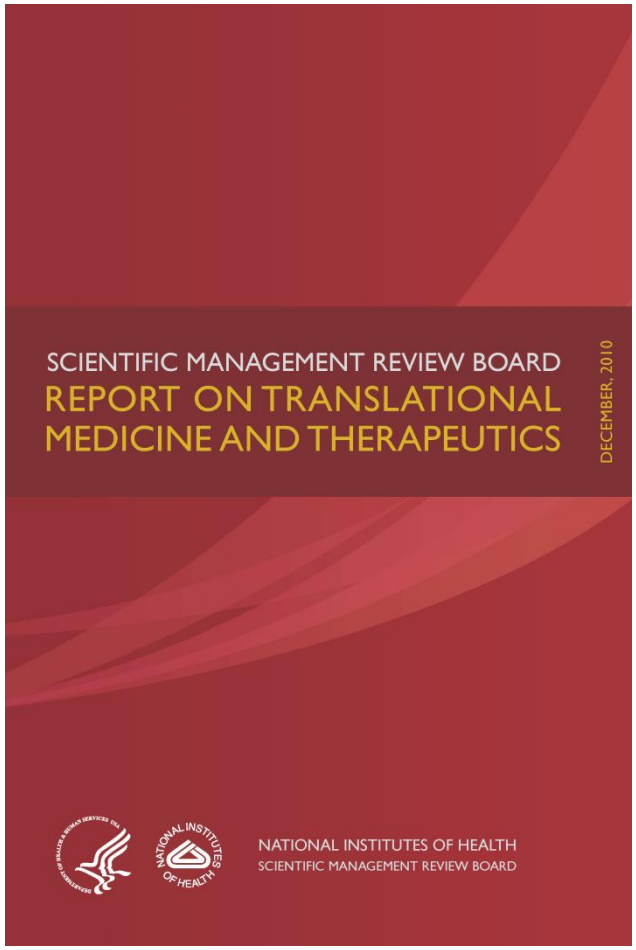
- Lovastatin (Mevacor)
- Imatinib (Gleevec)
- Paclitaxel (Taxol)
- Sunitib (Sutent)
- Abciximab (ReoPro)
- Filgrastim (Neupogen)
- The HPV vaccine Gardasil
- Ganciclovir (Vitrasert)
- Ketoconazole (Nizoral)

medpage TODAY

Conclusions

Public-sector research has had a more immediate effect on improving public health than was previously realized.

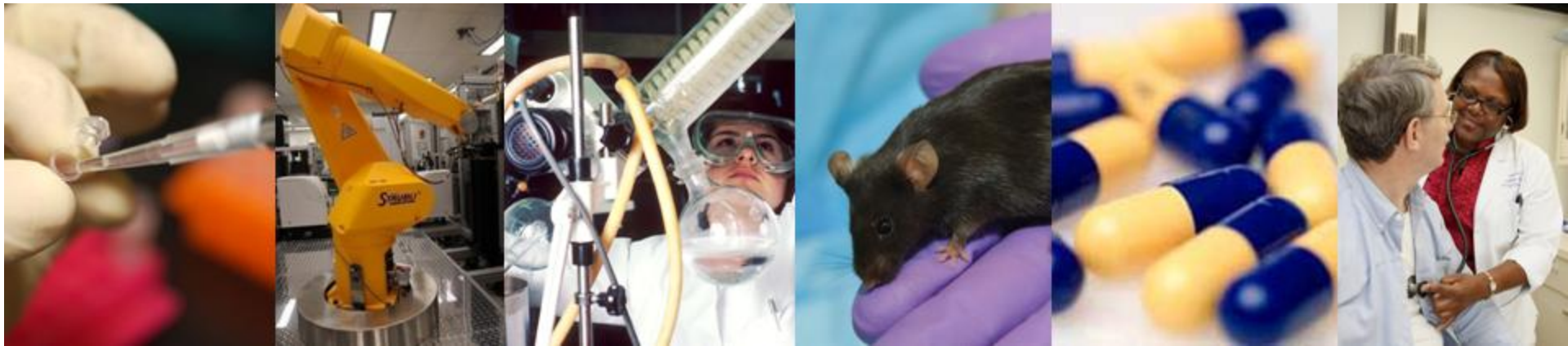
Scientific Management Review Board (SMRB) Recommendations to NIH



- May 2010
  - NIH Director Francis Collins asks SMRB to determine how NIH could better support translational and therapeutic sciences.
- December 2010
  - SMRB recommends (12 to 1) that a new translational medicine and therapeutics center be created.
  - SMRB also recommends NIH undertake a more extensive and detailed analysis through a transparent process to evaluate the new center's impact.

Creation of the National Center for Advancing Translational Sciences (NCATS)

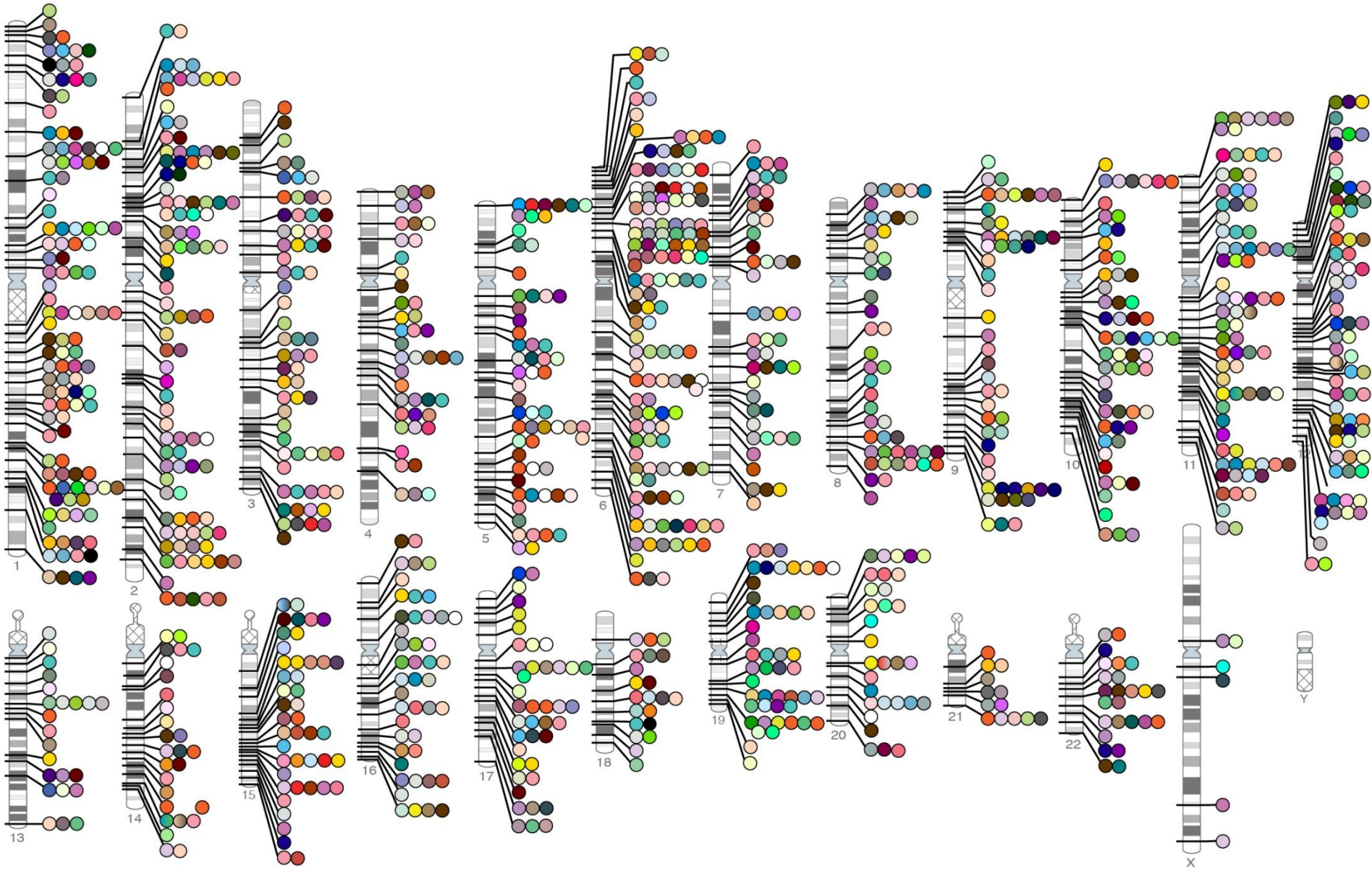
To advance the discipline of translational science and catalyze the development and testing of novel diagnostics and therapeutics across a wide range of human diseases and conditions



NCATS: Challenges & Opportunities

- Deluge of new discoveries of potential targets
- Unmet therapeutic needs for many conditions, especially rare and neglected diseases
- Need to view drug development pipeline as a scientific problem – ripe for experimentation and process engineering

Genetic Variants Associated with Disease Risk



www.genome.gov/GWAStudies

NCATS: Challenges & Opportunities

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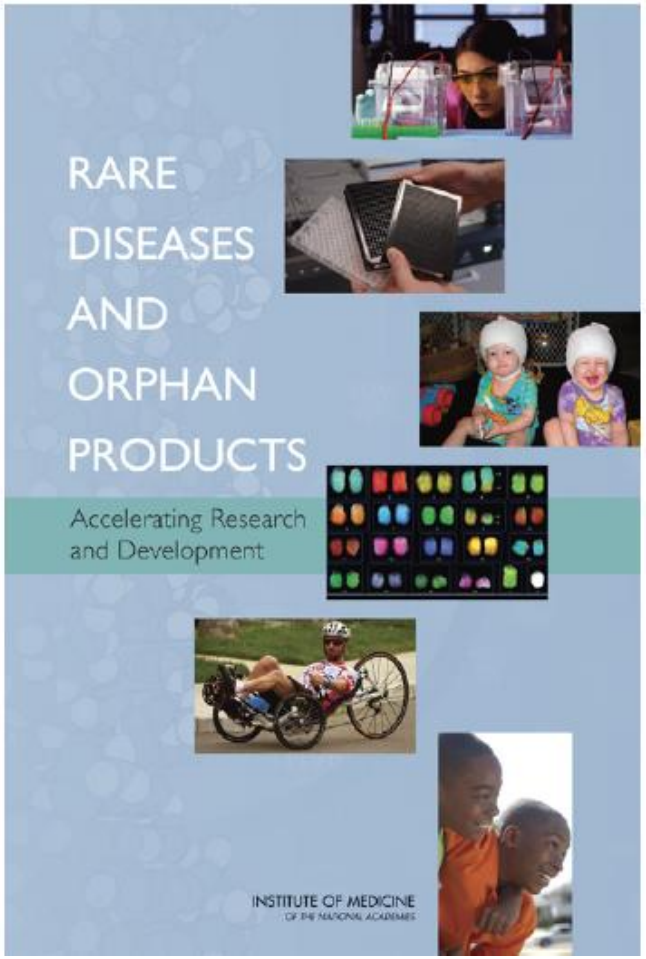

Elements of an Integrated National Strategy to Accelerate Research and Product Development for Rare Diseases

- Active involvement and collaboration by a wide range of public and private interests, including government agencies, commercial companies, academic institutions and investigators, and advocacy groups
- Timely application of advances in science and technology that can make rare diseases research and product development faster, easier, and less expensive
- Creative strategies for sharing research resources and infrastructure to make good and efficient use of scarce funding, expertise, data, biological specimens, and participation in research by people with rare diseases
- Appropriate use and further development of trial design and analytic methods tailored to the special challenges of conducting research on small populations
- Reasonable rewards and incentives for private-sector innovation and prudent use of public resources for product development when the latter appears a faster or less costly way to respond to important unmet needs
- Adequate organizations and resources, including staff with expertise on rare diseases research and product development, for the public agencies that fund biomedical research and regulate drugs and medical devices
- Mechanisms for weighing priorities for rare diseases research and product development, establishing collaborative as well as organization-specific goals, and assessing progress toward these goals

NCATS: Challenges & Opportunities

- Deluge of new discoveries of potential targets
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NCATS: Functions

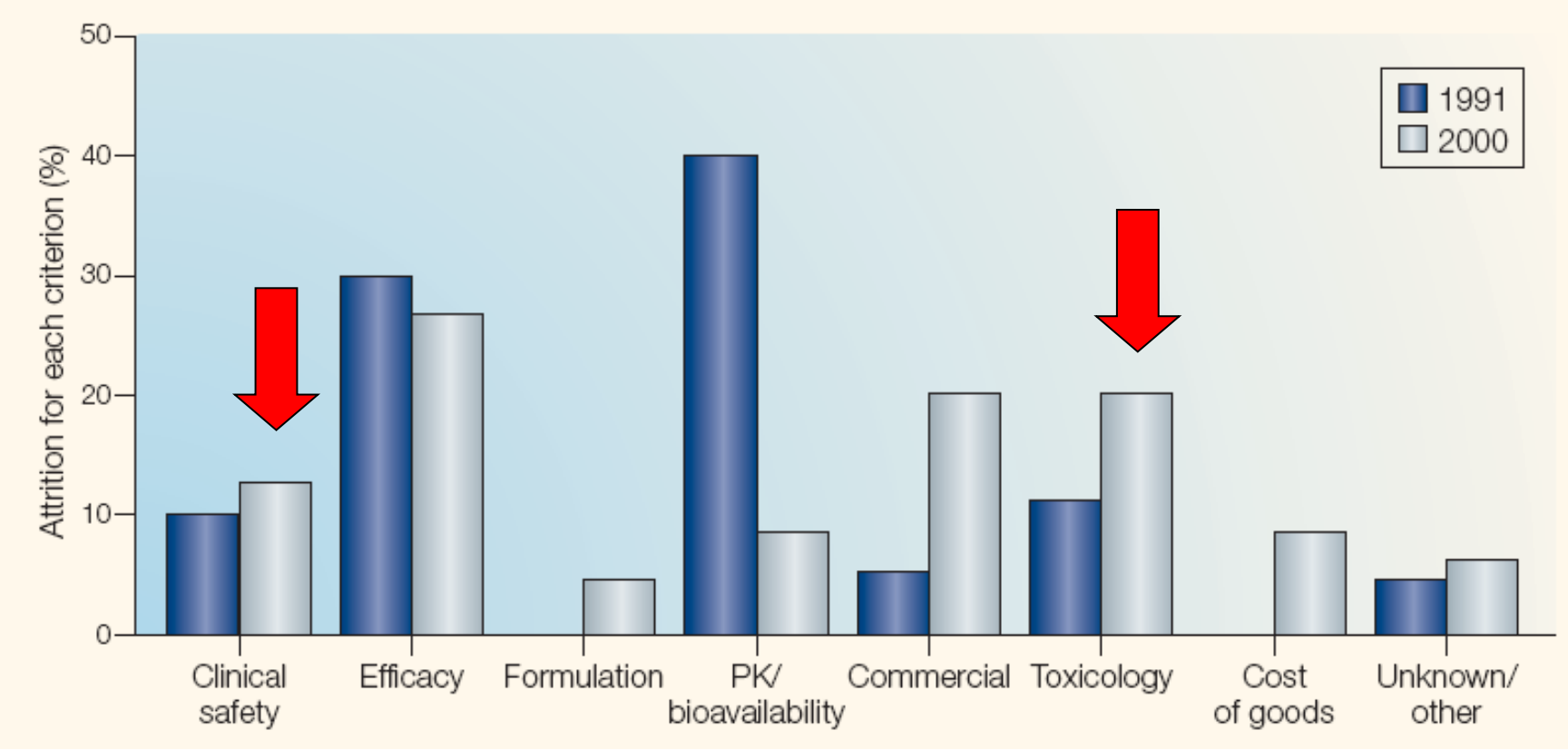
To improve processes in the therapeutics development pipeline by:

- Experimenting with innovative approaches along the pipeline utilizing an open-access model
- Choosing therapeutic projects to test innovative approaches
- Promoting interactions to advance regulatory science

To catalyze development of novel diagnostics and therapeutics by:

- Encouraging collaborations, partnerships across all sectors
- Providing resources to enable therapeutic development
- Enhancing training in relevant disciplines

Toxicity is the Most Common Reason for Drug Development Failure

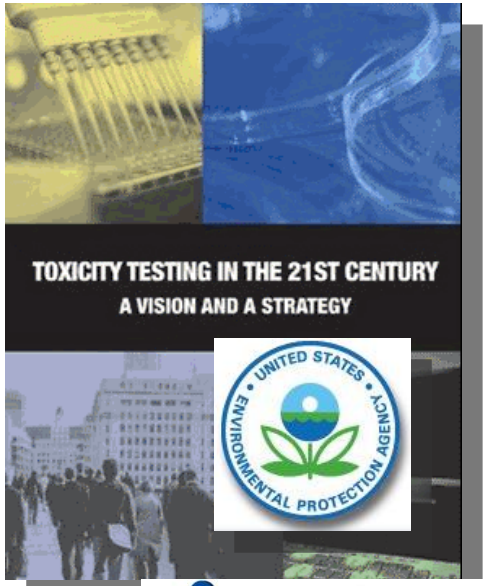


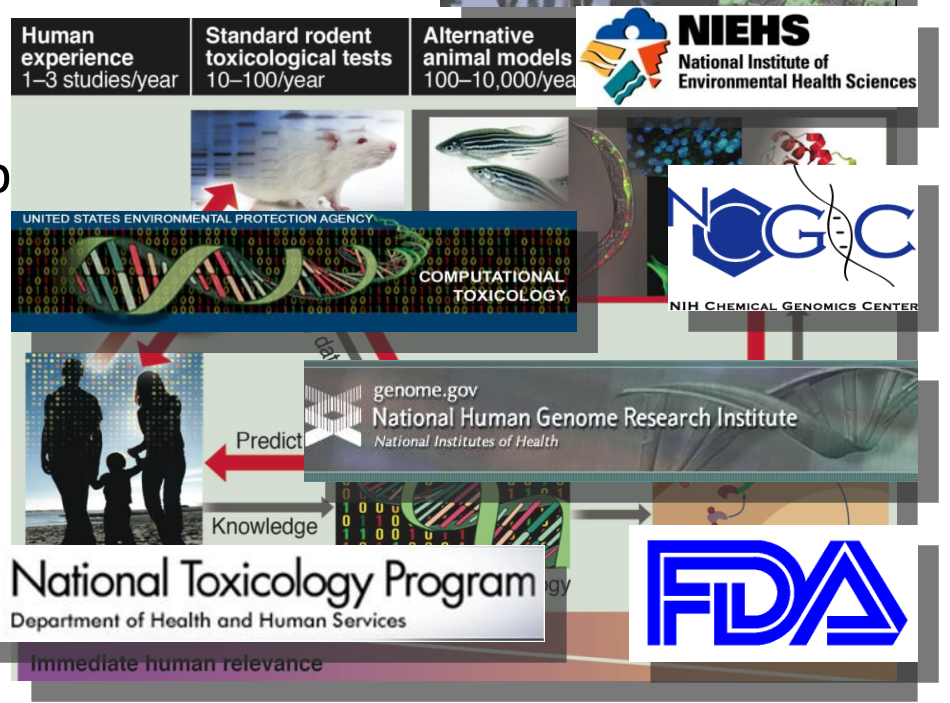
Preclinical (21%) + Clinical (12%) Tox = 33% of all failures

Kola and Landis, *Nature Reviews Drug Discovery* 3, 711-716, 2004.

Toxicology in the 21st Century (Tox21) Consortium

- A vision – and implementation strategy – to create a major shift in the assessment of chemical hazard and risk
  - Develop new approaches for safety assessment
  - Reduce animal use in toxicology
  - Transform toxicology from observational to predictive
- Collaborative effort (est. 2008) b
  - NIH
  - FDA
  - EPA
- Public access to all data





Tox21 Accomplishments

- Phase I (2008-2010): Proof-of-concept studies completed and published using 2800 compound library
  - Compounds profiled (qHTS) in >100 assays
- Phase II (2011- present)
  - 11,000 compound collection assembled including all approved drugs
  - Dedicated robotic platform created that profiles 11K library at 15 concentrations in triplicate in different assay every week
  - Relational map of all pathways operative in human cells created to allow assay prioritization
  - Informatics tools created for data analysis, dissemination, and predictive *in vitro* signature model-building
  - Targeted testing of compounds to follow up primary *in vitro* signatures and test their predictiveness *in vivo*

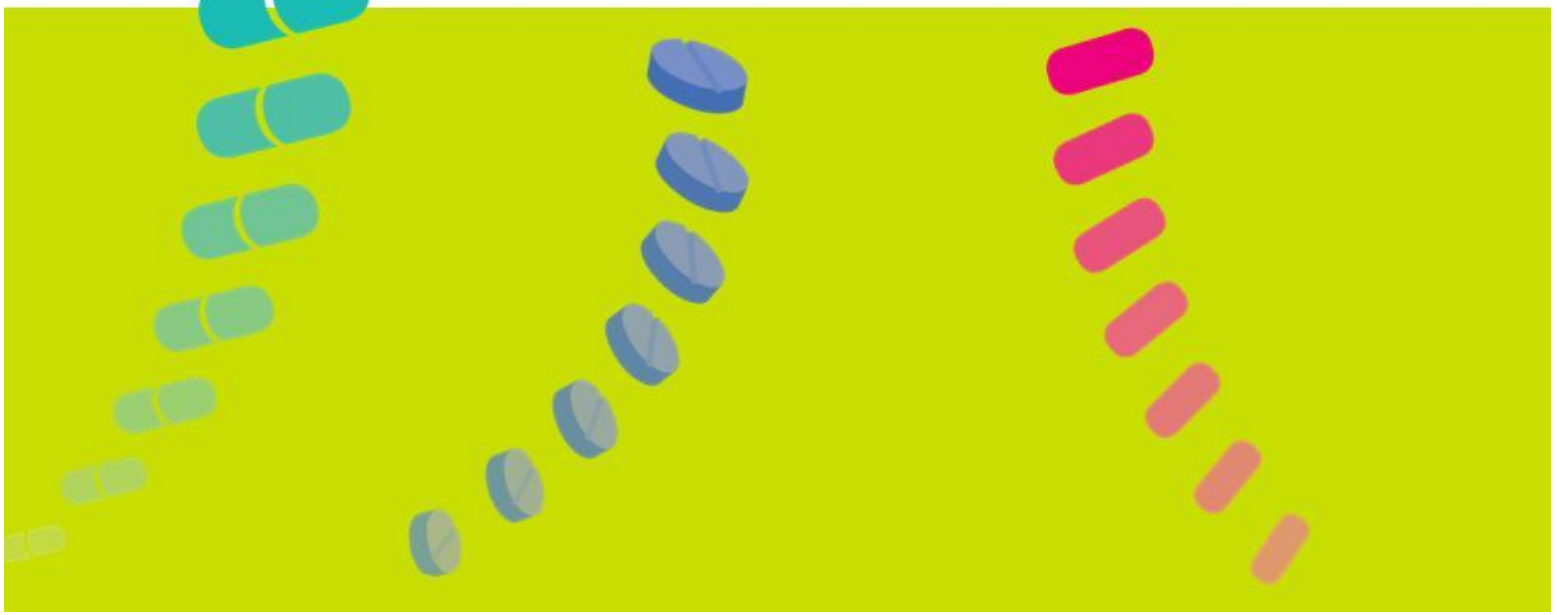
Public Access to the Tox21 Data

- ACToR – http://actor.epa.gov
  - Aggregated Computational Toxicology Resource
  - Data on chemicals of environmental interest from hundreds of sources
- CEBS - http://tools.niehs.nih.gov/cebs3/ui/
  - Chemical Effects in Biological Systems
  - Displays data in the context of biology and study design, and permits data integration across studies for novel meta analysis
- PubChem - http://pubchem.ncbi.nlm.nih.gov/
  - Free database of chemical structures of small organic molecules and information on their biological activities
  - Linked with NIH PubMed/Entrez information

NIH – INDUSTRY ROUNDTABLE

April 21–22, 2011

Exploring New Uses for Abandoned and Approved Therapeutics



NIH – INDUSTRY ROUNDTABLE

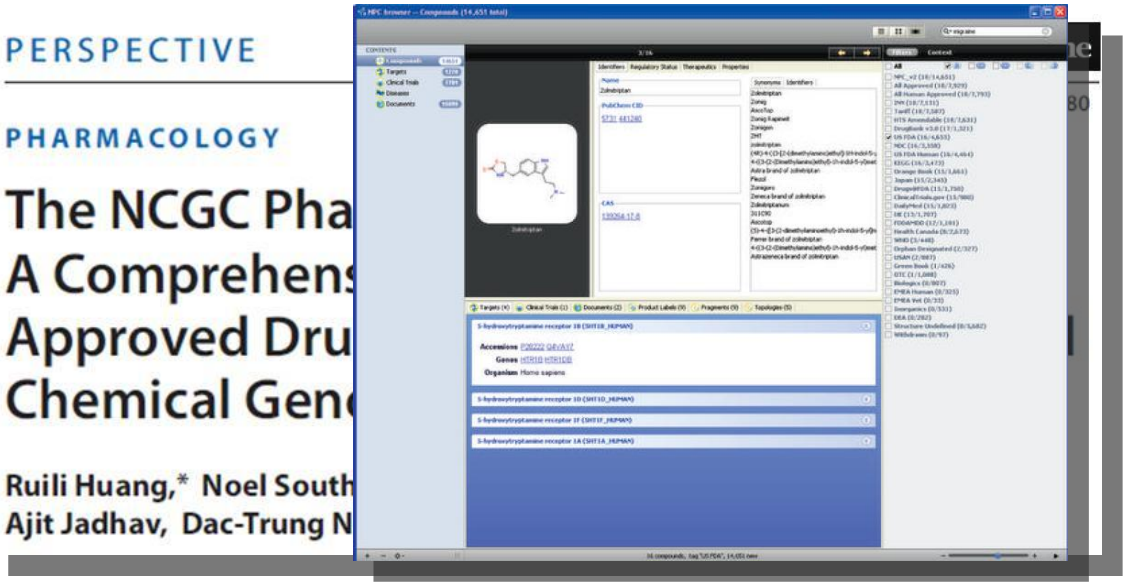
April 21–22, 2011

Exploring New Uses for Abandoned and Approved Therapeutics

- Participants: DHHS; academic institutions; industry; non-profit organizations
- *Goal:* Improve understanding of the landscape for drug rescue and repurposing by:
  - Examining model cases
  - Seeking new applications for current government activities
  - Exploring partnerships possibilities
  - Evaluating issues and opportunities
  - Establishing framework agreement for access to materials and data

All the (Approved) Drugs: A Definitive List

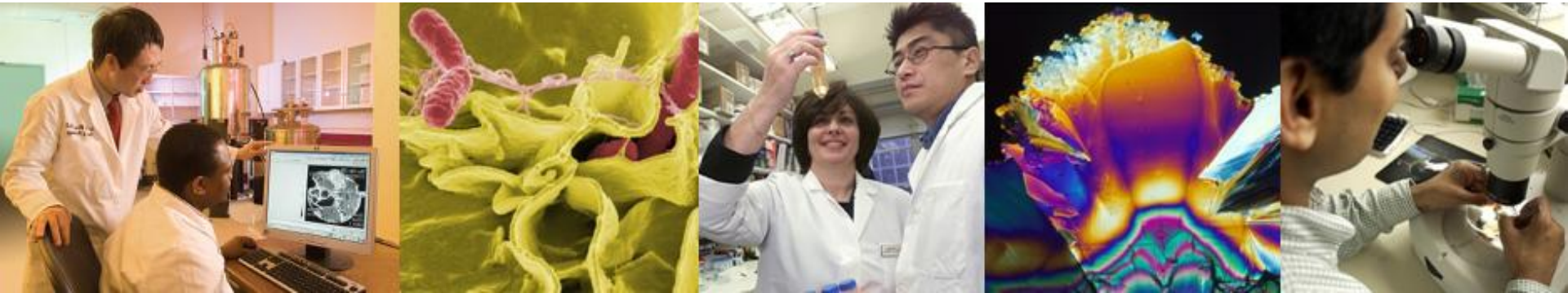
- NIH Chemical Genomics Center (NCGC): national resource for translating genomic information into biological insights and new therapeutics
- NPC: NCGC Pharmaceutical Collection
  - Definitive list of all small-molecule drugs approved for human or veterinary use (U.S. and worldwide)
  - NPC database browser: all data generated by NPC made publically available
- Purpose: facilitate und
  repurposing – especiall



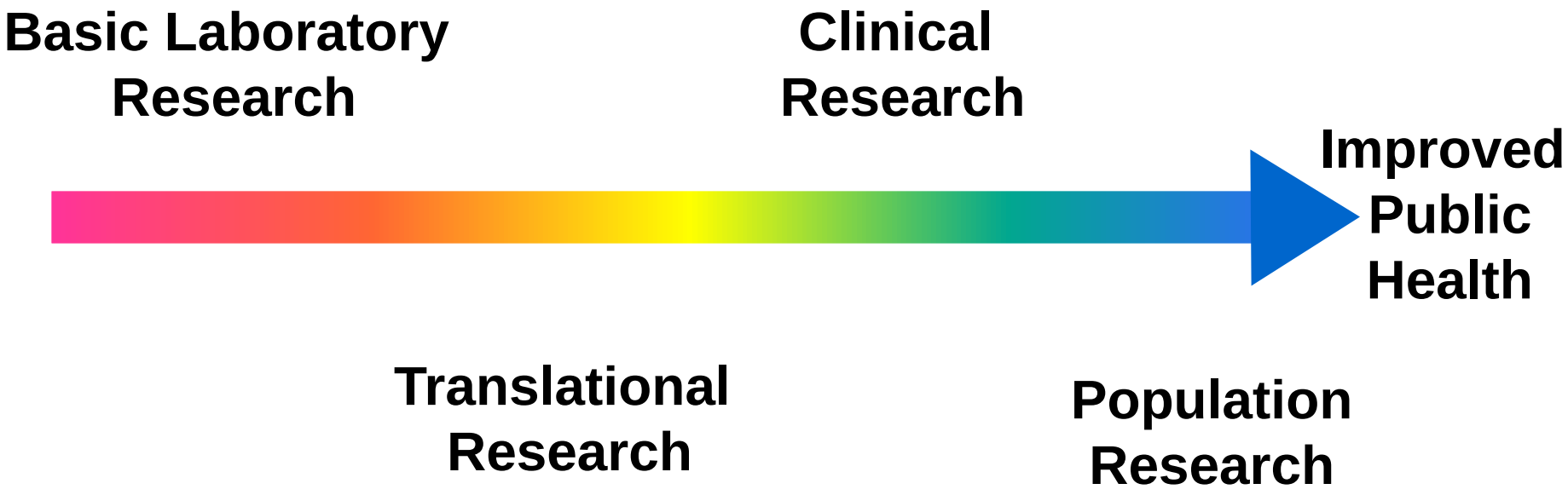
NIH Chemical Genomics Center

NCATS will:

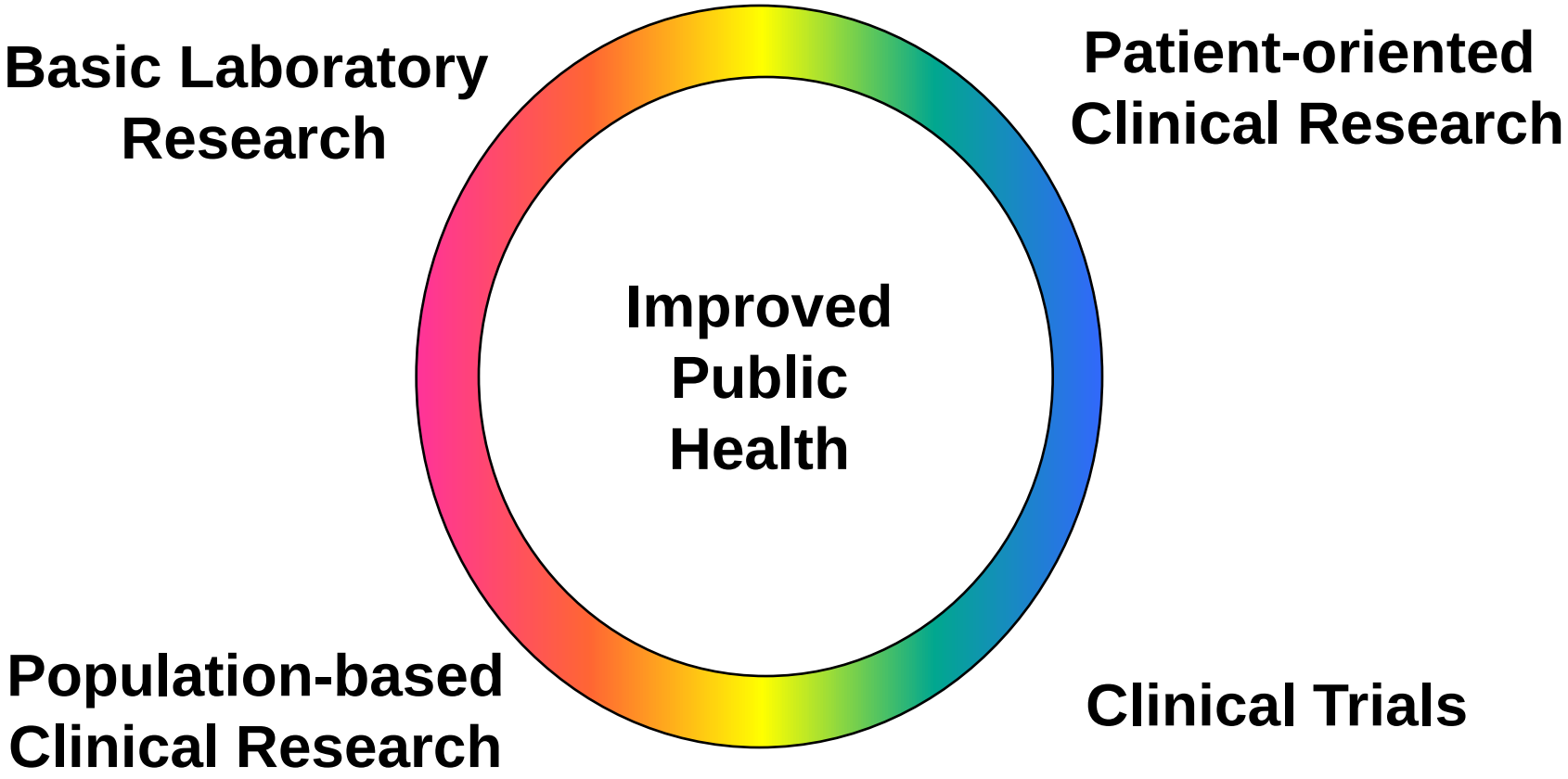
- Facilitate – not duplicate – other translational research activities supported by NIH
- Complement – not compete with – the private sector
- Reinforce – not reduce – NIH's commitment to basic research



Standard Model



The Way it Should Work



NCATS: Research Programs

- Components of Molecular Libraries Program
- Therapeutics for Rare and Neglected Diseases
- Office of Rare Diseases Research
- Rapid Access to Interventional Development
- Clinical and Translational Science Awards
- FDA-NIH Regulatory Science
- Cures Acceleration Network

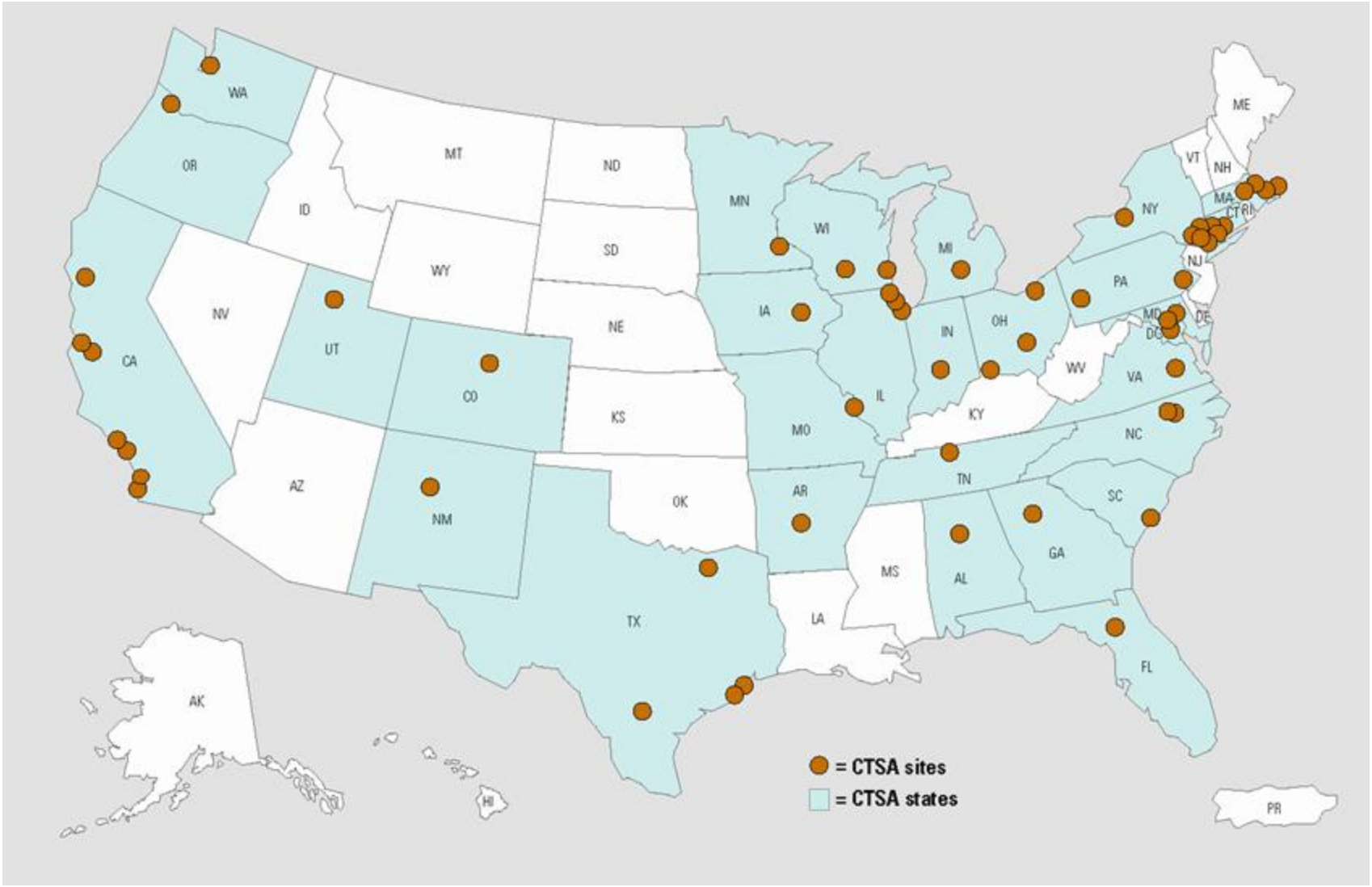
Molecular Libraries Program (MLP)

- Aims to enhance chemical biology efforts through high throughput screening (HTS) to obtain small molecule probes effective at modulating a given biological process or disease state. Includes:
  - Molecular Libraries Probe Production Centers Network (MLPCN) is a network of national laboratories that offer biomedical researchers access to HTS, secondary screens, and medicinal chemistry capacity
  - NIH Chemical Genomics Center (NCGC) facilitates early stage drug development in basic research laboratory and preclinical setting

Rapid Access to Interventional Development (RAID) Program

- Successful projects gain access to the government's contract resources and assistance from NIH in establishing and implementing a product development plan
- Services available include production, bulk supply, GMP manufacturing, formulation, development of an assay suitable for pharmacokinetic testing, and animal toxicology
- Additional assistance is provided during the regulatory process through access to independent product development planning expertise

Clinical and Translational Science Awards



NIH Therapeutics for Rare and Neglected Diseases (TRND) Program

- Creating a Drug Development Pipeline at NIH
- Congressionally-mandated effort to speed development of new drugs for rare and neglected diseases
- Collaboration between NIH-intramural and extramural labs with appropriate expertise
- Projects will:
  - Enter TRND at a variety of stages of development
  - Be taken to phase needed for external organization to adopt for clinical development
  - Not duplicate Pharma projects
- TRND will encourage creative partnerships; novel approaches to intellectual property

TRND Pilot Projects

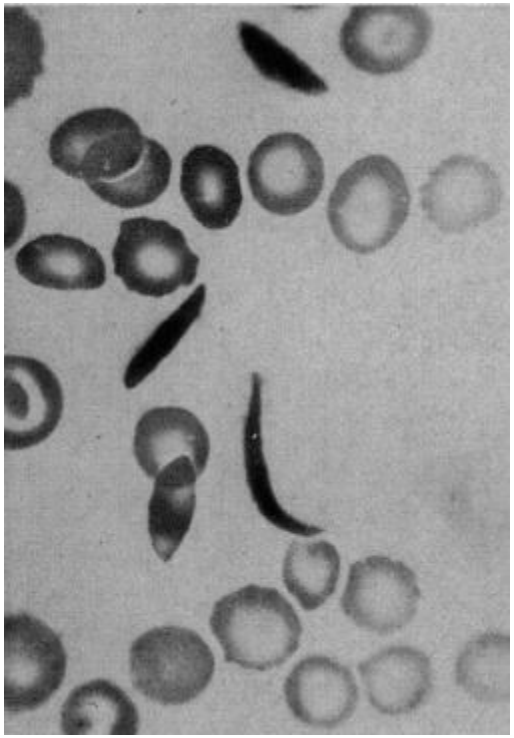
Disease	Type	Pathology	Collaborators	Compound type	Stage
Schistosomiasis, Hookworm	Neglected	Infectious parasite	Extramural	NME	Lead optimization
Niemann Pick C	Rare	CNS, liver/spleen	Disease Fnd, Extramural, Intramural	Repurposed approved drug	Preclinical
Hereditary Inclusion Body Myopathy	Rare	Muscle	Biotech, Intramural	Intermediate replacement	IND-enabling studies
Sickle Cell Disease	Rare	Blood	Biotech, Intramural	NME	IND-enabling studies & clinical trials design
Chronic Lymphocytic Leukemia	Rare	Cancer	Disease Fnd, Extramural	Repurposed approved drug	Pre-IND

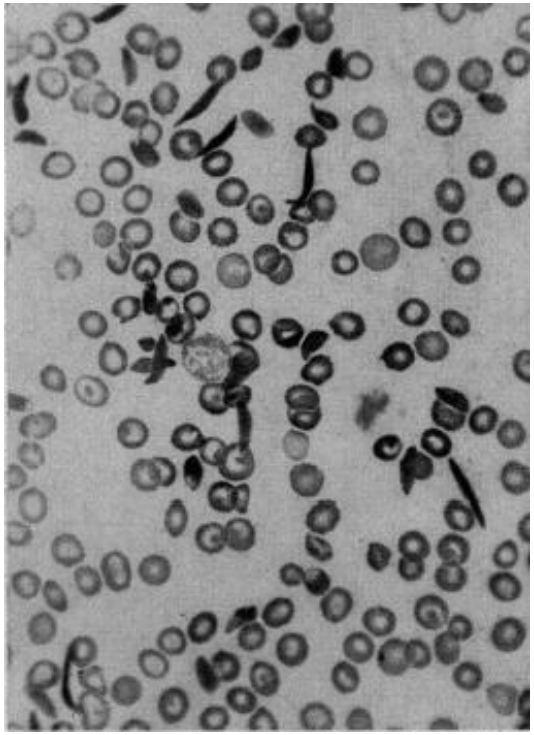
Centenary: 1910 Discovery of Sickle Cell Anemia

Archives of Internal Medicine (1910) vol. 5

PECULIAR ELONGATED AND SICKLE-SHAPED RED BLOOD CORPUSCLES IN A CASE OF SEVERE ANEMIA

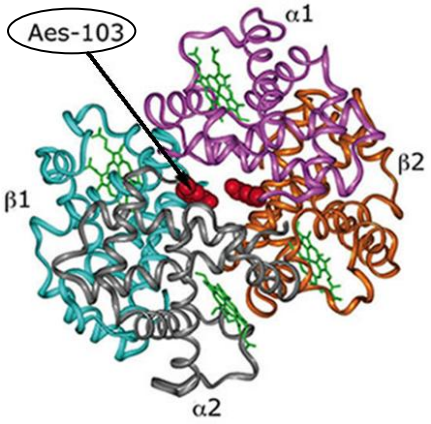
JAMES B. HERRICK, M.D.

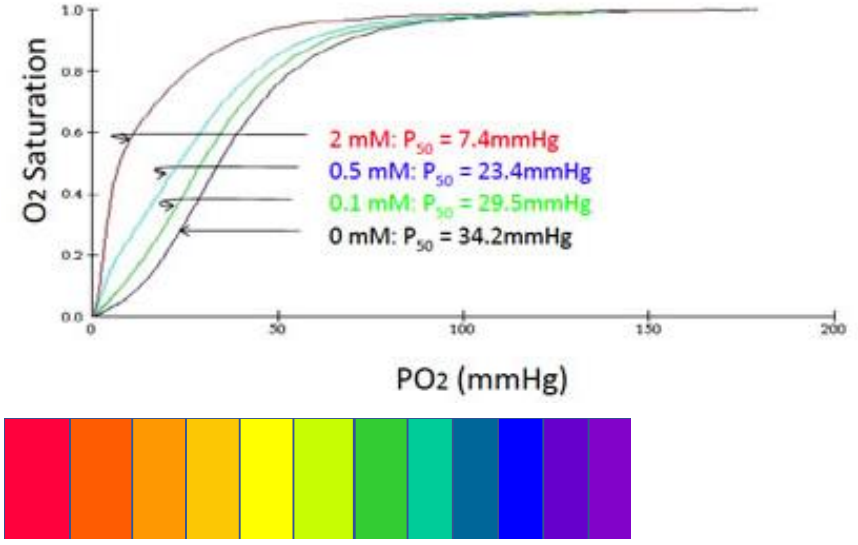


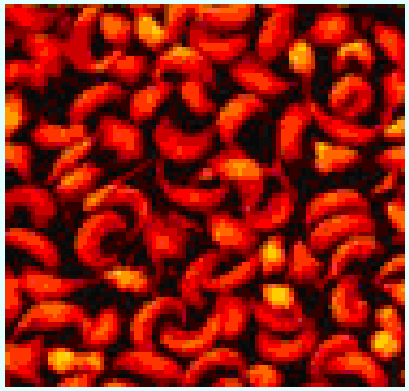


Therapeutics for Rare and Neglected Diseases (TRND): Pilot Project on SCD

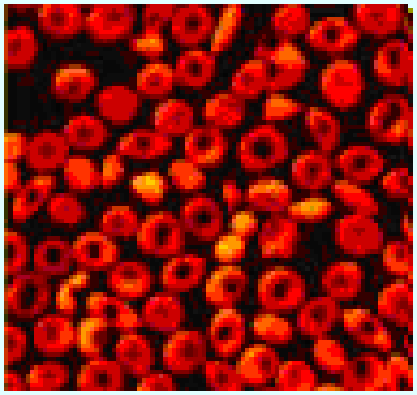
- Collaborator: AesRx, Boston-based biotech
- Compound: 5-hydroxymethyl-2-furfural (Aes-103)
  - Binds to sickle hemoglobin and increases its oxygen affinity
- Stage of project: late preclinical







Aes-103 0mM
almost all cells underwent sickling



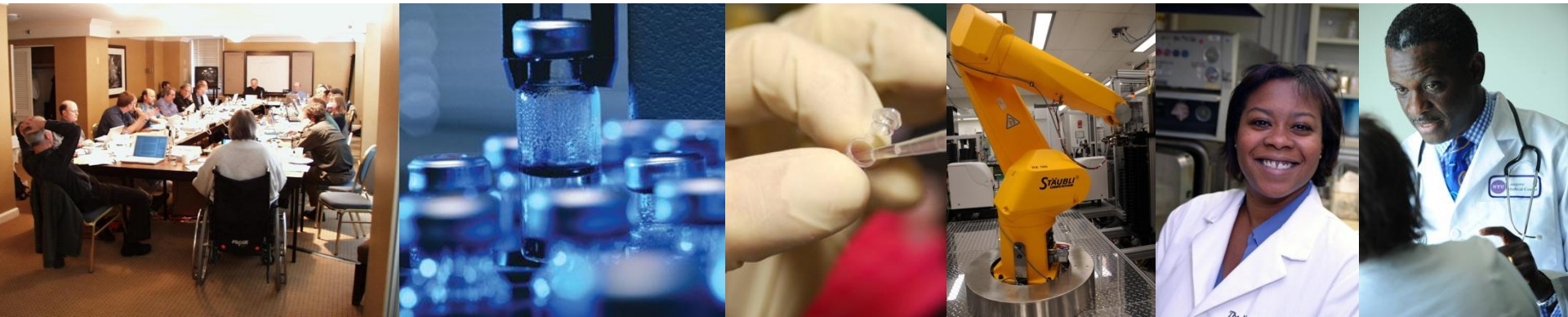
Aes-103 5mM
almost no sickled cells except some ISCs

New NIH-FDA Partnership

- NIH-FDA Joint Leadership Council
  - First meeting held October 28, 2010
- Joint Regulatory Science Initiative
  - 58 applications received
  - 4 projects funded
    - Diverse areas of research: Nanotechnology, heart-lung models for testing safety and efficacy, innovative clinical trial design, innovations in toxicological screening

Cures Acceleration Network (CAN)

- Established by the Affordable Care Act
- CAN will
  - Advance the development of “high need cures”
  - Reduce barriers between research discovery and clinical trials in areas that the private sector is unlikely to pursue in an adequate or timely way
- Review board will advise NIH Director
  - 24 members, including representatives from academia, private industry, and patient advocacy groups



NCATS: Planning Process

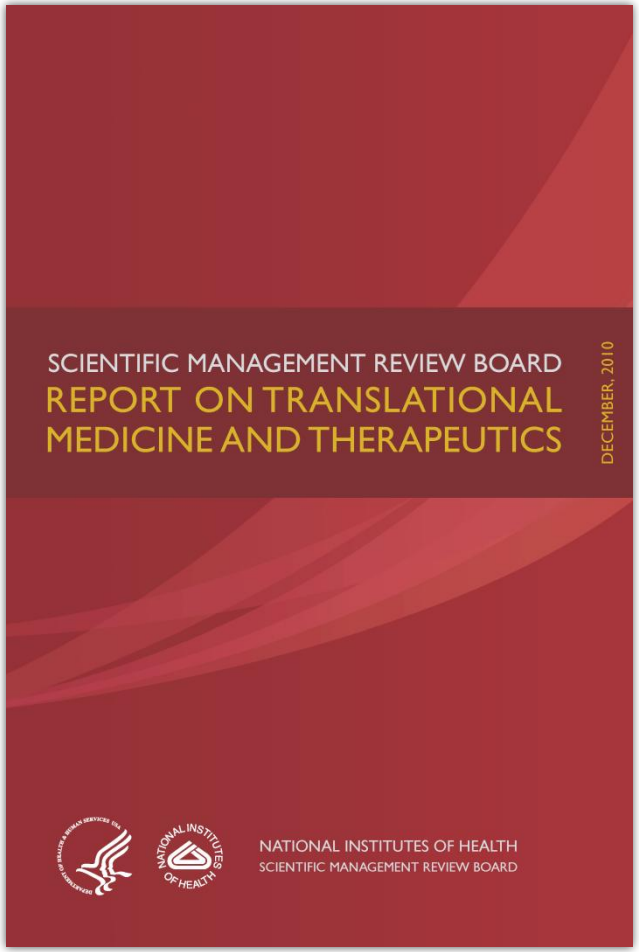
NIH Director established three panels to guide planning:

- Institute and Center Directors' NCATS Working Group
  - Presented recommendations on NCATS mission, functions, and organization to NIH Director on Feb. 17, 2011
- Advisory Committee to the Director (ACD) NCATS Working Group
  - Asked to provide high-level advice on how NCATS can best engage the private sector in translational science
  - Will report findings to full ACD later this year
- NIH Clinical and Translational Science Awards (CTSA) Integration Working Group
  - Formed in March 2011 to facilitate transition of CTSAs into NCATS

NCATS: Integrating Clinical and Translational Science Awards (CTSAs)

- CTSA Working Group Members
  - NIH Institute and Center leaders with extensive experience interacting with CTSAs
  - Senior staff from NIH Office of the Director
- Charge
  - Enumerate CTSA roles and capabilities that can support and enhance the NCATS mission
  - Identify CTSA needs and priorities that should be considered by NIH and NCATS leadership
  - Propose processes for ensuring smooth transitions
- In carrying out its charge, the Working Group will consult with CTSA leadership

Scientific Management Review Board (SMRB) Recommendations to NIH



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  - SMRB also recommends NIH undertake a more extensive and detailed analysis through a transparent process to evaluate the new center's impact.

NCRR Task Force Analysis

- The Task Force concurred with the SMRB recommendation to propose transfer of the CTSA program from NCRR to the proposed new Center, NCATS.
- The Task Force concluded that many of the programs that would remain in NCRR after the proposed CTSA transfer would benefit from the enhanced scientific adjacency that would be achieved by transfer of these programs to other Institutes or Centers.
- Informed by input from NCRR leadership and NCRR subject matter experts, a “straw model” was released on January 16th, 2011 to facilitate planning of potential transfers by providing a framework that stakeholders across NIH and from the extramural community comment on.
- The NCRR Task Force reported the results of its analysis to the SMRB on February 23rd. The final recommendations were released on March 1st, 2011.
- Proposed program and staff changes are planned to take effect October 1, 2011 (FY 2012).

Task Force Considerations and Guiding Principles

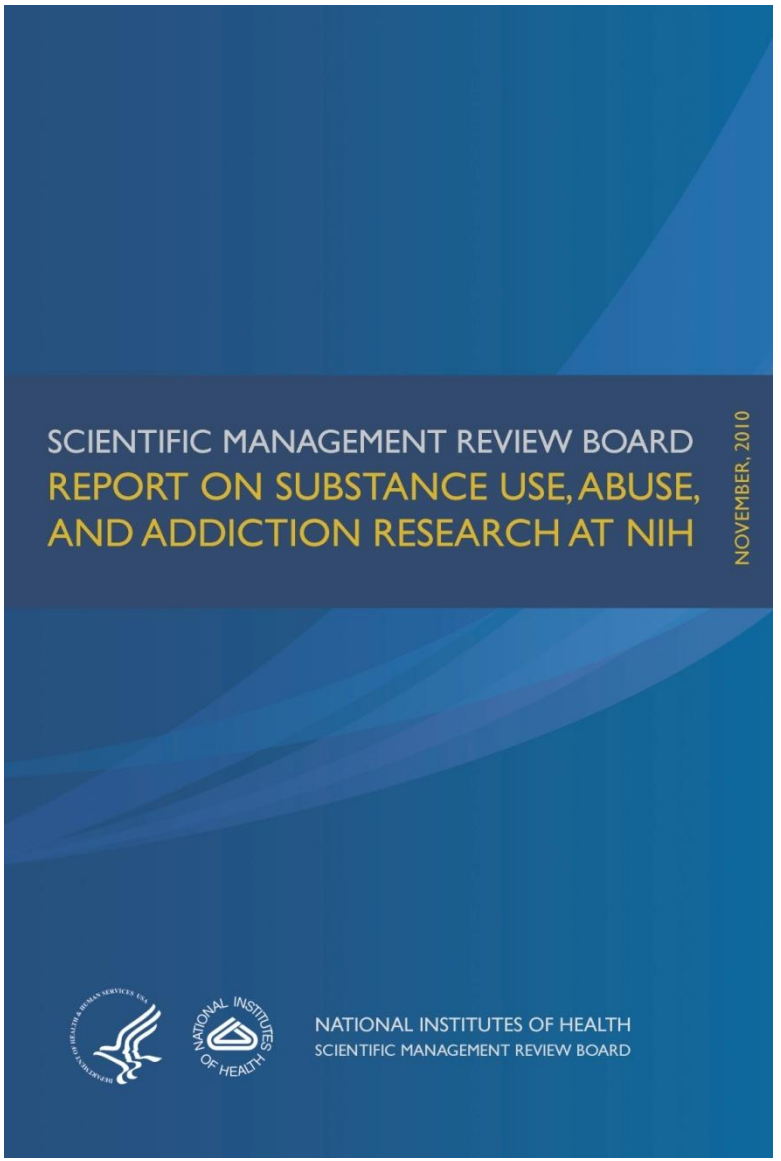
1. An assessment of the potential scientific synergies that could be achieved by placing the NCRR program in adjacency to the existing (or in the case of NCATS, proposed) portfolio/mission of the recipient IC versus the level of synergy among the existing NCRR programs.
2. The presumed “goodness of fit” or existing organizational niche for the NCRR program within the recipient IC versus the potential negative effects of adding a program that is disproportionately large and/or not well aligned to the recipient IC’s current (or in the case of NCATS, proposed) mission.
3. The potential level of disruption to long-standing NCRR programs led by dedicated NCRR staff versus the potential for disruptive innovation by reassigning NCRR staff to enable interactions with new colleagues and/or new programs.

NCRR Task Force Recommendations

Placement	Program
NCATS	• Clinical and Translational Science Awards (CTSA)
NIBIB	• Imaging and Point-of-Care Biomedical Technology Research Centers (BTRC) grants • Biomedical Imaging and Point-of-Care research grants for Technology Research and Development and SBIR/STTR grants
NIDDK	• Pancreatic Islet Cell Resource Center
NIGMS	• Institutional Development Awards (IDeA) • All other BTRC grants • All other research grants for Technology Research and Development, and the SBIR/STTR and BIRN network grants
NIMHD	• Research Centers in Minority Institutions program (RCMI)
OD	• Science Education Partnership Awards (SEPA)
Infrastructure Entity	• Comparative Medicine Program • Extramural Construction and Animal Facilities Improvement • Shared and High-End Instrumentation

NIH: Future, Plans, Priorities

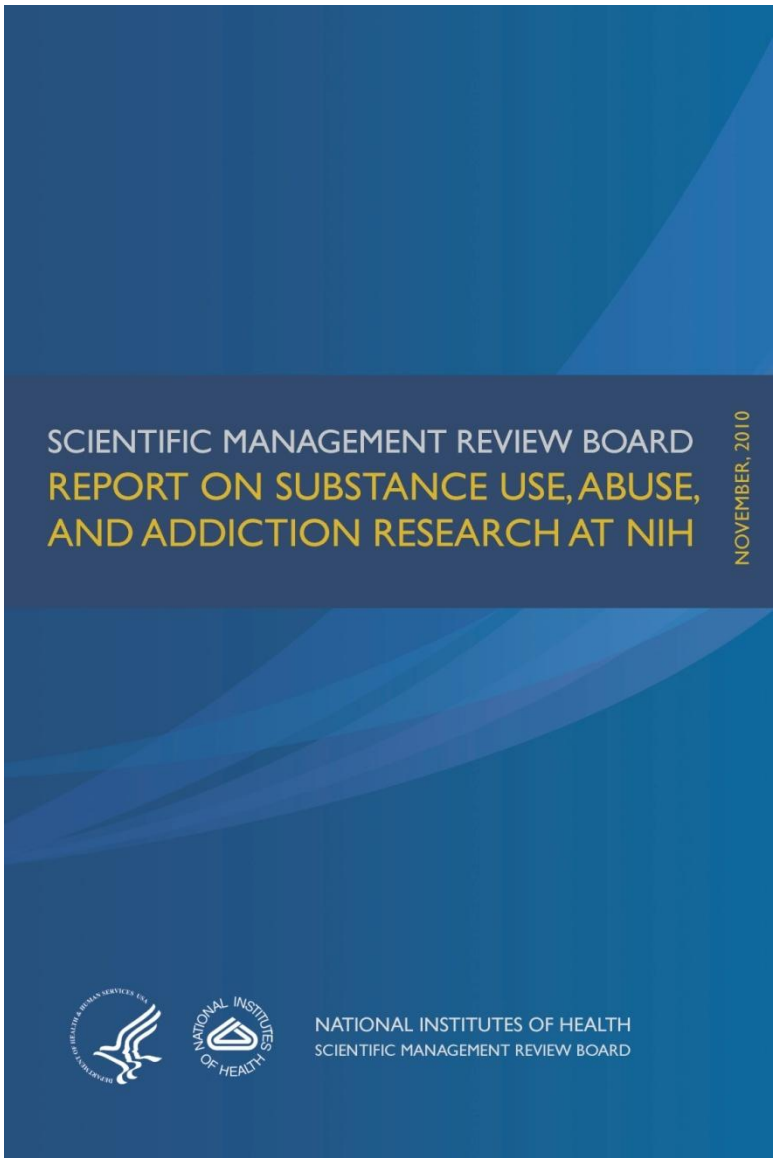
- Why Research Matters
- Translational and Therapeutics Research at NIH
- **Substance Use, Abuse, and Addiction Research at NIH**



SMRB Recommendations

Recommendation made on November 16, 2010 to:

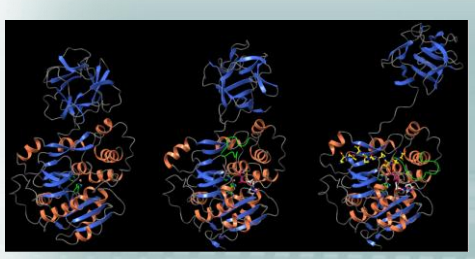
- Create a new Institute focusing on substance use, abuse, and addition research and related public health initiatives
- Integrate the relevant research portfolios from NIDA, NIAAA, and other ICs



Next Steps and Timeframe

- A SUAA Task Force has been analyzing all programs within NIAAA and NIDA and all SUAA programs across the NIH.
- This Task Force will provide final interim recommendations to the NIH director by the Fall of 2011. These recommendations will be informed by feedback by all relevant stakeholders.
- If approved, the new Institute would begin on October 1st, 2012 (FY 2013).

Tell us what you think…

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